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GC Nexis™ GC -2030

Application News

Analysis of Residual Ethylene Oxide in Medical Devices by Gas Chromatography

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User Benefits

- The simultaneous analysis of ethylene oxide (EO), ethylene chlorohydrin (ECH), and ethylene glycol (EG), which are residues by EOG sterilization, is possible.
- The requirements of gas chromatograph measurements for EO and ECH described in JIS T 0993-7: 2012 were satisfied.

■ Introduction

Ethylene oxide gas (EOG) is a flammable and colorless gas commonly used for medical device sterilization. Its permitted maximum residual levels are set by a range of international and local organizations, including the International Organization for Standardization (i.e., ISO 10993-7:2008) and Japanese Industrial Standards (i.e., JIS T 0993-7:2012).

EOG sterilization produces not only ethylene oxide (EO) residues, but also secondary compounds such as ethylene chlorohydrin (ECH) and ethylene glycol (EG) during the sterilization process. In these standards, allowable limits are specified for EO and ECH. Extraction can be either exhaustive or simulated-use. Exhaustive extraction entails a solvent extraction and allows a choice between the following two instrument configurations: the gas chromatograph (GC) and the headspace (HS) -GC.

In this article, the simultaneous analysis of EO, ECH, and EG by GC was performed with reference to JIS T 0993-7:2012, assuming a simulated-use or exhaustive extraction with water as an extraction solvent.

■ Preparation of Standard Solution

As the standard stock solution, a 100 µg/mL EO solution (P/N: 1021-31309, manufactured by GL Sciences Inc.) and a 500 µg/mL mixed solution of ECH and EG prepared by our division were prepared.

Four calibrator points were prepared by diluting the 500 µg/mL mixture of ECH and EG with water to final concentrations of 1, 5, 10, and 25 µg/mL, and cooling in a refrigerator. Then, a suitable amount of a 100 µg/mL EO solution cooled in a refrigerator was added to each concentration of the ECH and EG mixed solution to prepare 4 levels of mixed standard solution (1, 5, 10, and 25 µg/mL mixed standard solution of EO, ECH, and EG).

Table 1 summarizes the preparation methods for standard solutions.

※ Given that EO is easily volatilized, mixed solutions of ECH and EG were prepared, and then an EO solution was added to make the final solution. In addition, in order to suppress an evaporative loss of EO, it should be noted that 1.5 mL vials were used for preparation, and all the above-mentioned solutions and lab apparatus used to handle those solutions were kept at a sub-ambient temperature during the preparation.

Table 1 Preparation Method of Standard Solution

Standard concentrations (µg/mL)	500 µg/mL ECH・EG mixed solution (µL)	Distilled water (µL)	100 µg/mL EO solution (µL)
1	3	1482	15
5	15	1410	75
10	30	1320	150
25	75	1050	375

■ Analysis Conditions

In this experiment, the analysis conditions were established with reference to JIS T 0993-7:2012 using the gas chromatograph Nexis GC-2030. The instrument configuration and analysis conditions for this experiment are listed in Table 2.

Table 2 Instrument Configuration and Analysis Conditions

Model	: Nexis GC-2030 + AOC-20i Plus
Detector	: FID-2030 flame ionization detector
Analytical Column	: SH-PolarWax (30 m × 0.53 mm I.D., d.f.= 1.00 µm) *1
Column Temperature	: 60 °C (3 min) – 20 °C/min – 200 °C (10 min) Total 20 min
Injection Temperature	: 250 °C
Injection Mode	: Split
Split Ratio	: 3
Carrier Gas	: N_2
Carrier Gas Controller	: Constant Linear Velocity
Linear Velocity	: 40 cm/sec
Detector Temperature	: 250 °C
Detector Gas	: H_2 32 mL/min, Air 200 mL/min
Make up Gas	: N_2 24 mL/min
Injection Volume	: 0.5 µL
Syringe	: Elastic Syringe, AOC (P/N: 221-49548) *2

*1 P/N: 221-75979-30

*2 Using an elastic syringe for AOC (P/N: 221-49548) equipped with a plunger made of titanium enables stable sample introduction.

In this analysis, 20 mg of deactivated glass wool (P/N: 221-48600) were packed into a split glass insert (P/N: 221-41444-84) at a position 20 mm from the top. By increasing the amount of wool compared to the default amount and placing the wool slightly above the default position, the peak shape was stabilized and reproducibility was improved.

■ Measurement Evaluation

JIS T 0993-7:2012 contains the following statements with respect to system requirements of EO and ECH measurement.

※ This standard does not specify allowable limits for EG in medical devices .

- Resolution between the peak adjacent to EO or ECH be not less than 2.0
- Tailing factor for EO and ECH be not more than 1.8
- Relative deviation of the standard curve (RSD) does not exceed 5 % for the range of standards used
- %RSD of the EO and ECH peak area does not exceed 5% for the range of the standards used
- Correlation coefficient of the calibration curve be greater than 0.95.

■ Chromatogram and Calibration Curve of Standard Solution

In this article, we performed a simultaneous analysis using the mixture of EO, ECH, and EG standard solution, and confirmed whether the requirements mentioned above were satisfied for EO and ECH. Similar reference data are provided for EG.

The chromatograms of the EO, ECH, and EG standard solutions are shown in Fig. 1, the enlarged chromatograms and calibration curves of EO, ECH, and EG are shown in Figs. 2, 3, and 4, and the detailed analytical results are summarized in Tables 3, 4, and 5 respectively.

From the results of the standard solutions, the requirements for EO and ECH were satisfied, and good analytical results were obtained.

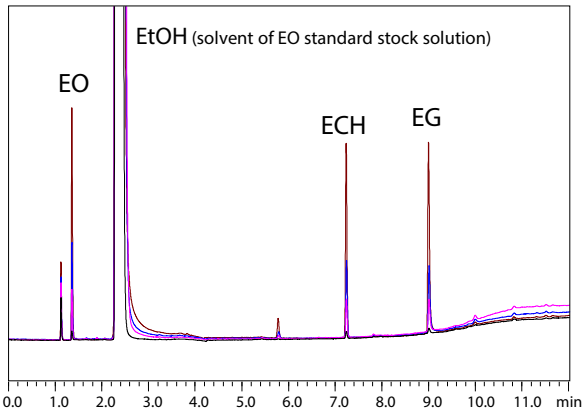

Fig. 1 Standard Chromatograms (0~12 min)

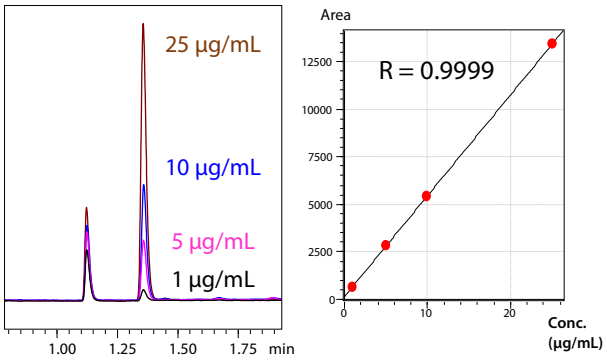

Fig. 2 Chromatogram and Calibration Curve of EO

Table 3 Analytical Results of EO (n=6) *1

Concentration (µg/mL)	1	5	10	25
Mean area value	653	2833	5426	13401
Area value %RSD	3.279	0.828	0.919	0.477
Resolution	6.304	6.520	6.508	6.411
Tailing factor	1.471	1.369	1.357	1.385
Limit of detection (µg/mL) *2	0.106	0.113	0.122	0.122
Limit of quantification (µg/mL) *2	0.355	0.377	0.407	0.407
S/N	27.9	136.8	245.7	642.5

*1 The chromatograms and analytical results are for reference purposes only and should not be regarded as guaranteed values.
*2 The limit of detection and the lower limit of quantification were calculated at S/N=3 and S/N=10, respectively.

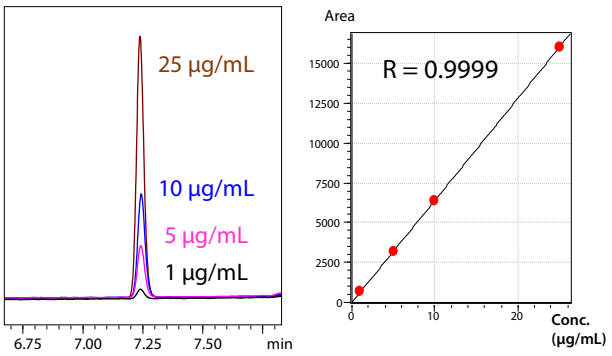

Fig. 3 Chromatogram and Calibration Curve of ECH

Table 4 Analytical Results of ECH (n=6) *1

Concentration (µg/mL)	1	5	10	25
Mean area value	632	3197	6384	16027
Area value %RSD	1.390	0.723	0.644	0.341
Resolution	65.77	23.34	23.18	23.21
Tailing factor	1.080	1.097	1.102	1.103
Limit of detection (µg/mL) *2	0.158	0.148	0.153	0.144
Limit of quantification (µg/mL) *2	0.527	0.494	0.511	0.479
S/N	19.6	103.2	196.0	545.9

*1 The chromatograms and analytical results are for reference purposes only and should not be regarded as guaranteed values.
*2 The limit of detection and the lower limit of quantification were calculated at S/N=3 and S/N=10, respectively.

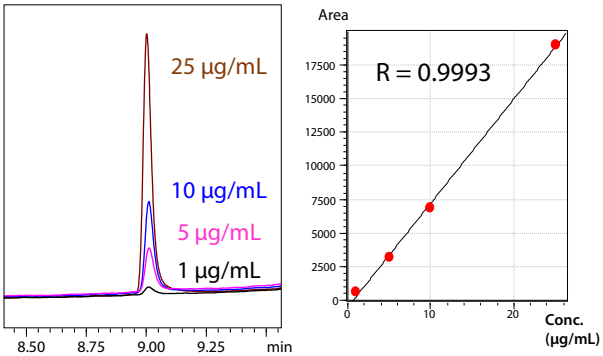

Fig. 4 Chromatogram and Calibration Curve of EG

Table 5 Analytical Results of EG (n=6) *1

Concentration (µg/mL)	1	5	10	25
Mean area value	578	3214	6884	19000
Area value %RSD	5.814	1.176	1.463	1.125
Resolution	21.73	27.86	28.36	29.03
Tailing factor	1.229	1.380	1.428	1.465
Limit of detection (µg/mL) *2	0.285	0.172	0.165	0.145
Limit of quantification (µg/mL) *2	0.952	0.575	0.550	0.484
S/N	15.4	85.3	174.2	543.0

*1 The chromatograms and analytical results are for reference purposes only and should not be regarded as guaranteed values.
*2 The limit of detection and the lower limit of quantification were calculated at S/N=3 and S/N=10, respectively.

※ EG is highly adsorptive and easily remains in syringes and inserts. The number of solvent washes was increased, and blank analysis was interposed between different samples.

■ Conclusion

Simultaneous analysis of EO, ECH, and EG residues by EOG sterilization was conducted by GC in reference to JIS T 0993-7:2012 and ISO 10993-7:2008. The Shimadzu Nexis GC-2030 satisfied the system requirements and is considered an excellent instrument for measuring residue in medical devices by EOG sterilization.

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